

Witherspoon 10/715,607

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:609952 CAPLUS

DOCUMENT NUMBER: 141:157893

ENTRY DATE: Entered STN: 30 Jul 2004

TITLE: Novel monofunctional polyethylene glycol aldehydes

useful for pegylation

INVENTOR(S): Rosen, Perry; Nho, Kwang

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S.

Ser. No. 661,268.

CODEN: USXXCO

DOCUMENT TYPE: LANGUAGE: Patent English

INT. PATENT CLASSIF.:

MAIN: C08G065-32

US PATENT CLASSIF.: 525389000; 525403000

CLASSIFICATION: 37-3 (Plastics Manufacture and Processing)

Section cross-reference(s): 63

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 2004147687	A1	20040729	US 2003-715607	20031118 <	_
KR 2003048293	A	20030619	KR 2001-78244	20011211	
US 2003153694	A1	20030814	US 2002-303260	20021125	
US 2004034188	A1	20040219	US 2003-431294	20030507	
US 6916962	B2	20050712		•	
US 2004122164	A1	20040624	US 2003-661268	20030912	
PRIORITY APPLN. INFO.:			KR 2001-78244	A 20011211	
•			US 2002-348452P	P 20020116	
			US 2002-381503P	P 20020517	
			US 2002-407741P	P 20020903	
			US 2002-303260	A2 20021125	
•			US 2003-431294	A2 20030507	
•			US '2003-661268	A2 20030912	

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004147687	ICM	C08G065-32
	INCL	525389000; 525403000
US 2004147687	NCL	525/389.000; 525/403.000
	ECLA	C08G065/324; C08G065/329; C08G065/331; C08G065/333U <
US 2003153694	NCL	525/523.000; 558/260.000; 560/157.000; 564/060.000
	ECLA	C08G065/329; C08G065/331; C08G065/333U
US 2004034188	NCL	528/230.000; 528/250.000
	ECLA	C08G065/324; C08G065/329; C08G065/331; C08G065/333U
US 2004122164	NCL	525/054.100; 528/230.000; 525/526.000
	ECLA	C08G065/324; C08G065/329; C08G065/331; C08G065/333U

ABSTRACT:

The present invention provides novel monofunctional polyethylene glycol aldehydes for the pegylation of therapeutically active proteins. The pegylated protein conjugates that are produced, retain a substantial portion of their therapeutic activity and are less immunogenic than the protein from which the conjugate is derived. New syntheses for preparing such aldehydes are described.

SUPPL TERM: polyethylene glycol aldehyde therapeutic active protein

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pegylation
                   Polyoxyalkylenes, preparation
INDEX TERM:
                   ROLE: IMF (Industrial manufacture); THU (Therapeutic use);
                   BIOL (Biological study); PREP (Preparation); USES (Uses)
                      (aldehyde derivs.; novel monofunctional polyethylene
                      glycol aldehydes for pegylation of therapeutically active
                      proteins)
INDEX TERM:
                   Proteins
                   ROLE: THU (Therapeutic use); BIOL (Biological study); USES
                   (Uses)
                      (pegylation of; novel monofunctional polyethylene glycol
                      aldehydes for pegylation of therapeutically active
                      proteins)
INDEX TERM:
                 6318-30-5P 58320-73-3P 67665-18-3P
                   , Methoxypolyethylene glycol acetic acid 67665-19-4P
                   , Methoxypolyethylene glycol ethyl acetate
                   124661-64-9P 135649-01-3P
                   146167-55-7P 544706-94-7P
                   544706-96-9P 544707-00-8P
                   544707-01-9P 544707-03-1P
                   544707-04-2P 544707-06-4P
                   658083-74-0P 658083-75-1P
                   727741-77-7P
                   ROLE: IMF (Industrial manufacture); RCT (Reactant); PREP
                   (Preparation); RACT (Reactant or reagent)
                      (novel monofunctional polyethylene glycol aldehydes for
                      pegylation of therapeutically active proteins)
INDEX TERM:
                 79-10-7DP, Acrylic acid, addition products with
                  methoxypolyethylene glycol, ester with hydroxysuccinimide,
                   amide derivative, urethane propionaldehyde 6066-82-6DP
                    N-Hydroxysuccinimide, ester with methoxypolyethylene
                   glycol acrylic acid addition product, amide derivative, urethane
                   propionaldehyde 9004-74-4DP, Methoxypolyethylene
                   glycol, addition products with acrylic acid, ester with
                   hydroxysuccinimide, amide derivative, urethane propionaldehyde
                   41365-75-7DP, displacement reaction products with
                   hydroxysuccinimide esterified methoxypolyethylene glycol
                   acrylic acid addition product, deacetalized compound
                   533881-58-2P 544706-95-8P
                   544706-97-0P 544706-99-2P
                   544707-02-0P 544707-05-3P
                   544708-06-7P
                   ROLE: IMF (Industrial manufacture); THU (Therapeutic use);
                   BIOL (Biological study); PREP (Preparation); USES (Uses)
                      (novel monofunctional polyethylene glycol aldehydes for
                      pegylation of therapeutically active proteins)
INDEX TERM:
                 67-64-1, Acetone, reactions 98-59-9, Tosyl
                   chloride 105-36-2, Ethyl bromoacetate
                  1659-31-0; Di-2-pyridyl carbonate 6066-82-6
                   , N-Hydroxysuccinimide 7693-46-1, 4-Nitrophenyl
                   chloroformate 9004-74-4, Methoxypolyethylene
                   glycol 14533-84-7, Pentafluorophenyl
                   trifluoroacetate 14697-46-2, Pentane-1,2,5-triol
                   19060-15-2 32315-10-9, Triphosgene
                   41365-75-7 80506-64-5 125220-94-2
                   , Methoxypolyethylene glycol propionic acid
                   ROLE: RCT (Reactant); RACT (Reactant or reagent)
```

(novel monofunctional polyethylene glycol aldehydes for

pegylation of therapeutically active proteins)

IT 6318-30-5P 58320-73-3P 67665-18-3P,

Methoxypolyethylene glycol acetic acid 67665-19-4P,

Methoxypolyethylene glycol ethyl acetate 124661-64-9P

135649-01-3P 146167-55-7P 544706-94-7P

544706-96-9P 544707-00-8P 544707-01-9P

544707-03-1P 544707-04-2P 544707-06-4P

658083-74-0P 658083-75-1P 727741-77-7P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(novel monofunctional polyethylene glycol aldehydes for pegylation of

therapeutically active proteins)

RN 6318-30-5 CAPLUS

CN 1,3-Dioxolane-4-propanol, 2,2-dimethyl- (9CI) (CA INDEX NAME)

RN 58320-73-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[(4-methylphenyl)sulfonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

$$MeO = \begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix} \begin{bmatrix} O \\ S \\ O \end{bmatrix}$$

RN 67665-18-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(carboxymethyl)- ω -methoxy- (9CI) (CA INDEX NAME)

RN 67665-19-4 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(2-ethoxy-2-oxoethyl)- ω -methoxy-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O \\
 & CH_2 - CH_2 - O \\
 & D \\$$

RN 124661-64-9 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[(4-nitrophenoxy)carbonyl]- ω -

the contract of the contract o

methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
O & & & \\
O - C & & & \\
\end{array}$$

$$\begin{array}{c|c}
O - CH_2 - CH_2 & & \\
\end{array}$$
OMe

RN 135649-01-3 CAPLUS

Poly(oxy-1,2-ethanediyl), α -[[(2,5-dioxo-1-CN pyrrolidinyl)oxy]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

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146167-55-7 CAPLUS RN

Poly(oxy-1,2-ethanediy1), α -methy1- ω -[2-[[(2-CNpyridinyloxy)carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

544706-94-7 CAPLUS RN

Poly(oxy-1,2-ethanediyl), α -[2-[(3,3-diethoxypropyl)amino]-2-CN oxoethyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544706-96-9 CAPLUS

Poly(oxy-1,2-ethanediy1), α -[3-[(4,4-dimethoxybuty1)amino]-3-CN oxopropyl]-ω-methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{O} & \text{OMe} \\ & \parallel & \parallel \\ \text{CH}_2 - \text{CH}_2 - \text{O} & \parallel \\ & \parallel & \parallel \\ \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_1 - \text{CH}_2) \ 3 - \text{CH} - \text{OMe} \\ \end{array}$$

RN 544707-00-8 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(4,4-dimethoxybutyl)amino]carbonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544707-01-9 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[2-[[[(3,3-diethoxypropyl)amino]carbonyl]amino]ethyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544707-03-1 CAPLUS

CN 1,3-Dioxolane-4-propanol, 2,2-dimethyl-, 4-nitrobenzoate (9CI) (CA INDEX NAME)

RN 544707-04-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[2-[[[3-(2,2-dimethyl-1,3-dioxolan-4-yl)propoxy]carbonyl]amino]ethyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544707-06-4 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[3-(2,2-dimethyl-1,3-dioxolan-4-yl)propyl]- ω -methoxy- (9CI) (CA INDEX NAME)

Me O (CH₂)₃
$$-$$
 O CH₂ $-$ CH₂ $-$ OMe

RN 658083-74-0 CAPLUS

Poly(oxy-1,2-ethanediyl), α -[3-(2,5-dioxo-1-pyrrolidinyl)-2-CNoxopropyl]-ω-methoxy- (9CI) (CA INDEX-NAME)

$$\begin{array}{c|c} CH_2-C-CH_2 & \boxed{} O-CH_2-CH_2 & \boxed{} OMe \\ \hline \\ N & O \end{array}$$

658083-75-1 CAPLUS RN

Poly(oxy-1,2-ethanediyl), α -[[(3,3-diethoxypropyl)amino]carbonyl]-CN ω-methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OEt} & \text{O} \\ \mid & \mid \\ \text{EtO-CH-CH}_2\text{-CH}_2\text{-NH-C} & \text{O-CH}_2\text{-CH}_2 & \text{OMe} \\ \end{array}$$

727741-77-7 CAPLUS RN

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[3-oxo-3-(pentafluorophenoxy)propoxy] - (9CI) (CA INDEX NAME)

IT 79-10-7DP, Acrylic acid, addition products with methoxypolyethylene glycol, ester with hydroxysuccinimide, amide derivative, urethane propionaldehyde 6066-82-6DP, N-Hydroxysuccinimide, ester with methoxypolyethylene glycol acrylic acid addition product, amide derivative, urethane propionaldehyde 9004-74-4DP, Methoxypolyethylene glycol, addition products with acrylic acid, ester with hydroxysuccinimide, amide derivative, urethane propionaldehyde 41365-75-7DP, displacement reaction products with hydroxysuccinimide esterified methoxypolyethylene glycol acrylic acid addition product, deacetalized compound 533881-58-2P 544706-95-8P 544706-97-0P

544706-99-2P 544707-02-0P 544707-05-3P

544708-06-7P

RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(novel monofunctional polyethylene glycol aldehydes for pegylation of therapeutically active proteins)

RN 79-10-7 CAPLUS

2-Propenoic acid (9CI) (CA INDEX NAME) CN

RN 6066-82-6 CAPLUS

CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)

RN 9004-74-4 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -hydroxy- (9CI) (CA INDEX NAME).

RN 41365-75-7 CAPLUS

CN 1-Propanamine, 3,3-diethoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{OEt} \\ | \\ \text{Eto-} \text{ CH-} \text{ CH}_2\text{--} \text{ CH}_2\text{--} \text{ NH}_2 \end{array}$$

RN 533881-58-2 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α-methyl-ω-(4-oxobutoxy)- (9CI) (CA INDEX NAME)

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OHC-
$$(CH_2)_3$$
-O- CH_2 - CH_2 -O n Me

RN 544706-95-8 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[2-oxo-2-[(3-oxopropyl)amino]ethoxy]- (9CI) (CA INDEX NAME)

RN 544706-97-0 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[3-oxo-3-[(4-oxobutyl)amino]propoxy]- (9CI) (CA INDEX NAME)

RN 544706-99-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(4-oxobutyl)amino]carbonyl]- ω -methoxy-(9CI) (CA INDEX NAME)

RN 544707-02-0 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[2-[[[(3-oxopropyl)amino]carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

RN 544707-05-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[2-[[(4-oxobutoxy)carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

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$$ch_2$$
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RN 544708-06-7 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(3-oxopropyl)amino]carbonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

IT 67-64-1, Acetone, reactions 98-59-9, Tosyl chloride 105-36-2, Ethyl bromoacetate 1659-31-0, Di-2-pyridyl carbonate 6066-82-6, N-Hydroxysuccinimide 7693-46-1, 4-Nitrophenyl chloroformate 9004-74-4, Methoxypolyethylene

glycol 14533-84-7, Pentafluorophenyl trifluoroacetate 14697-46-2, Pentane-1,2,5-triol 19060-15-2

32315-10-9, Triphosgene 41365-75-7 80506-64-5

125220-94-2, Methoxypolyethylene glycol propionic acid

RL: RCT (Reactant); RACT (Reactant or reagent) (novel monofunctional polyethylene glycol aldehydes for pegylation of therapeutically active proteins)

RN67-64-1 CAPLUS

2-Propanone (9CI) (CA INDEX NAME) CN

RN 98-59-9 CAPLUS

Benzenesulfonyl chloride, 4-methyl- (9CI) (CA INDEX NAME) CN

105-36-2 CAPLUS RN

Acetic acid, bromo-, ethyl ester (6CI, 8CI, 9CI) (CA INDEX NAME) CN

1659-31-0 CAPLUS RN

CN2-Pyridinol, carbonate (2:1) (ester) (9CI) (CA INDEX NAME)

6066-82-6 CAPLUS RN

2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME) CN

RN 7693-46-1 CAPLUS

CN Carbonochloridic acid, 4-nitrophenyl ester (9CI) (CA INDEX NAME)

RN 9004-74-4 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -hydroxy- (9CI) (CA INDEX NAME)

HO
$$CH_2$$
 CH_2 O CH_3

RN 14533-84-7 CAPLUS

CN Acetic acid, trifluoro-, pentafluorophenyl ester (7CI, 8CI, 9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
F & O \\
O - C - CF_3
\end{array}$$

RN 14697-46-2 CAPLUS

CN 1,2,5-Pentanetriol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 19060-15-2 CAPLUS

CN 1-Butanamine, 4,4-dimethoxy- (9CI) (CA INDEX NAME)

RN 32315-10-9 CAPLUS

CN Methanol, trichloro-, carbonate (2:1) (9CI) (CA INDEX NAME)

RN 41365-75-7 CAPLUS

CN 1-Propanamine, 3,3-diethoxy- (9CI) (CA INDEX NAME)

RN 80506-64-5 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(2-aminoethyl)- ω -methoxy- (9CI) (CA INDEX NAME)

MeO
$$CH_2-CH_2-O$$
 $CH_2-CH_2-NH_2$

RN 125220-94-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(2-carboxyethyl)- ω -methoxy- (9CI) (CA INDEX NAME)

MeO
$$CH_2 - CH_2 - O$$
 $CH_2 - CH_2 - CH_2 - CO_2H_2$

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:513373 CAPLUS

DOCUMENT NUMBER:

141:72062

ENTRY DATE:

Entered STN: 25 Jun 2004

TITLE:

__monofunctional polyethylene glycol aldehydes,

preparation and protein conjugate

INVENTOR(S):

Rosen, Perry; Nho, Kwang H.

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S.

Pat. Appl. 2004 34,188.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

INT. PATENT CLASSIF.:

MAIN:

C08G065-00

SECONDARY:

C08G063-48; C08G063-91

US PATENT CLASSIF.: CLASSIFICATION:

525054100; 528230000; 525526000

CLASSIFICATION: 35-8 (Chemistry of Synthetic High Polymers)
Section cross-reference(s): 63

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.		KIND	DATE	APPLICATION NO.	DATE
US 200412216 KR 200304829 US 200315369	US 2004122164 KR 2003048293 US 2003153694 US 2004034188			US 2003-661268 KR 2001-78244 US 2002-303260 US 2003-431294	20030912 20011211 20021125
US 2004147687 PRIORITY APPLN. INFO.:		B2 A1	20040729	US 2003-715607 KR 2001-78244 US 2002-303260 US 2003-431294	A 20011211 A2 20021125 A2 20030507
PATENT CLASSIFICA				US 2002-348452P US 2002-381503P US 2002-407741P US 2003-661268	P 20020517 P 20020903
	CLASS	PATENT		SIFICATION CODES	
US 2004122164	ICM ICS INCL	C08G065	-00 -48; C08G06		
US 2004122164	NCL ECLA	525/054 C08G065	.100; 528/2 /324; C08G0	30.000; 525/526.000 65/329; C08G065/331;	
US 2003153694 US 2004034188	NCL ECLA NCL	C08G065		60.000; 560/157.000; 65/331; C08G065/333U	
US 2004147687	ECLA	C08G065		65/329; C08G065/331;	C08G065/333U
ABSTRACT:	ECLA		•	65/329; C08G065/331;	
The monofunctional polyethylene glycol aldehydes are used for the pegylation of therapeutically active proteins. The pegylated protein conjugates that are produced, retain a substantial portion of their therapeutic activity and are less immunogenic than the protein from which the conjugate is derived.					
SUPPL. TERM: INDEX TERM:	Prote ROLE:	eins : BUU (B	iological u	<pre>ehyde pegylated prot se, unclassified); E</pre>	
<pre>study); USES (Uses)</pre>					
INDEX TERM: Polyoxyalkylenes, preparation ROLE: BUU (Biological use, unclassified); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses) (polyethylene glycol aldehydes for conjugates with					
proteins) INDEX TERM: 14697-46-2, Pentane-1,2,5-triol ROLE: RCT (Reactant); RACT (Reactant or reagent) (cyclization; polyethylene glycol aldehydes for conjugates with proteins)					
INDEX TERM:	112344- copol amino 53388 54470 54470	-11-3DP, lymer, r odiethox 31-58-2P 06-97-0P	Acrylic ac eaction pro ypropane, a 544706-95- 544707-05-	id-ethylene oxide gr ducts with hydroxysu nd aldehyde formatic 8P 2P	ıccinimide,
	~ ~ ~ ~ / (•	

```
ROLE: IMF (Industrial manufacture); PREP (Preparation)
     (polyethylene glycol aldehydes for conjugates with
                     proteins)
                67665-19-4P 92451-01-9P
INDEX TERM:
                  544706-94-7P 544706-96-9P
                  544706-98-1P 544707-00-8P
                  544707-01-9P 544707-04-2P
                  544707-06-4P
                  ROLE: IMF (Industrial manufacture); RCT (Reactant); PREP
                  (Preparation); RACT (Reactant or reagent)
                      (polyethylene glycol aldehydes for conjugates with
                     proteins)
                1659-31-0, Di-2-pyridyl carbonate 9004-74-4
INDEX TERM:
                  , Methoxypolyethylene glycol
                  ROLE: RCT (Reactant); RACT (Reactant or reagent)
                     (polyethylene glycol aldehydes for conjugates with
                     proteins)
INDEX TERM:
                135649-01-3P 146167-55-7P
                  ROLE: IMF (Industrial manufacture); RCT (Reactant); PREP
                  (Preparation); RACT (Reactant or reagent)
                     (reaction with aminodiethoxypropane; polyethylene glycol
aldehydes for conjugates with proteins)
INDEX TERM:
                124661-64-9P 174569-25-6P
                  ROLE: IMF (Industrial manufacture); RCT (Reactant); PREP
                  (Preparation); RACT (Reactant or reagent)
                      (reaction with aminodimethoxybutane; polyethylene glycol
                     aldehydes for conjugates with proteins)
INDEX TERM:
                58320-73-3P
                  ROLE: IMF (Industrial manufacture); RCT (Reactant); PREP
                  (Preparation); RACT (Reactant or reagent)
                     (reaction with dioxolanedimethylpropanol; polyethylene
                     glycol aldehydes for conjugates with proteins)
INDEX TERM:
                80506-64-5
                  ROLE: RCT (Reactant); RACT (Reactant or reagent)
                     (reaction with dipyridiyl carbonate; polyethylene glycol
                     aldehydes for conjugates with proteins)
INDEX TERM:
                67665-18-3P
                  ROLE: IMF (Industrial manufacture); RCT (Reactant); PREP
                  (Preparation); RACT (Reactant or reagent)
                      (reaction with hydroxysuccinimide; polyethylene glycol
                     aldehydes for conjugates with proteins)
INDEX TERM: 125220-94-2
                  ROLE: RCT (Reactant); RACT (Reactant or reagent)
                      (reaction with hydroxysuccinimide; polyethylene glycol
                     aldehydes for conjugates with proteins)
INDEX TERM:
                6066-82-6, N-Hydroxysuccinimide
                  ROLE: RCT (Reactant); RACT (Reactant or reagent)
                     (reaction with methoxypolyethylene glycol acetic acid;
                     polyethylene glycol aldehydes for conjugates with
                     proteins)
INDEX TERM:
                544707-03-1P
                  ROLE: IMF (Industrial manufacture); RCT (Reactant); PREP
                  (Preparation); RACT (Reactant or reagent)
                      (reaction with methoxypolyethylene glycol aminoethyl
                     ether; polyethylene glycol aldehydes for conjugates with
                     proteins)
INDEX TERM:
                19060-15-2
                  ROLE: RCT (Reactant); RACT (Reactant or reagent)
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(reaction with methoxypolyethylene glycol succinimidyl
                      acetal; polyethylene glycol aldehydes for conjugates with
                     proteins)
                 41365-75-7
INDEX TERM:
                   ROLE: RCT (Reactant); RACT (Reactant or reagent)
                      (reaction with methoxypolyethylene glycol succinimidyl
                      acetate; polyethylene glycol aldehydes for conjugates
                     with proteins)
INDEX TERM:
                 105-36-2, Ethyl bromoacetate 7693-46-1,
                   4-Nitrophenylchloroformate 32315-10-9, Triphosgene
                   ROLE: RCT (Reactant); RACT (Reactant or reagent)
             (reaction with methoxypolyethylene glycol; polyethylene
                     glycol aldehydes for conjugates with proteins)
                6318-30-5
INDEX TERM:
                   ROLE: RCT (Reactant); RACT (Reactant or reagent)
                      (reaction with nitrophenylchloroformate; polyethylene
                      glycol aldehydes for conjugates with proteins)
IT
     14697-46-2, Pentane-1,2,5-triol
    RL: RCT (Reactant); RACT (Reactant or reagent)
       (cyclization; polyethylene glycol aldehydes for conjugates with
       proteins)
     14697-46-2 CAPLUS
    1,2,5-Pentanetriol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
CN
        ОН
HO-CH_2-CH-(CH_2)_3-OH
    112344-11-3DP, Acrylic acid-ethylene oxide graft copolymer,
reaction products with hydroxysuccinimide, aminodiethoxypropane, and
    aldehyde formation 533881-58-2P 544706-95-8P
     544706-97-0P 544706-99-2P 544707-02-0P
     544707-05-3P 544708-06-7P
    RL: IMF (Industrial manufacture); PREP (Preparation)
        (polyethylene glycol aldehydes for conjugates with proteins)
RN
    112344-11-3 CAPLUS
    2-Propenoic acid, polymer with oxirane, graft (9CI) (CA INDEX NAME)
CN
    CM
         1
    CRN 79-10-7
    CMF C3 H4 O2
HO-C-CH-CH2
    CM
    CRN 75-21-8
    CMF C2 H4 O
```

RN 533881-58-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -(4-oxobutoxy)- (9CI) (CA INDEX NAME)

OHC-
$$(CH_2)_3$$
-O- CH_2 - CH_2 -O- n Me

RN 544706-95-8 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -methyl- ω -[2-oxo-2-[(3-oxopropyl)amino]ethoxy]- (9CI) (CA INDEX NAME)

RN 544706-97-0 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[3-oxo-3-[(4-oxobutyl)amino]propoxy]- (9CI) (CA INDEX NAME)

RN 544706-99-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(4-oxobutyl)amino]carbonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

OHC-
$$(CH_2)_3$$
-NH-C- O- CH_2 - CH_2 - OMe

RN 544707-02-0 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[2-[[[(3-oxopropyl)amino]carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

RN 544707-05-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[2-[[(4-oxobutoxy)carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

RN 544708-06-7 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[(3-oxopropyl)amino]carbonyl]-ωmethoxy- (9CI) (CA INDEX NAME)

IT 67665-19-4P 92451-01-9P 544706-94-7P 544706-96-9P 544706-98-1P 544707-00-8P

544707-01-9P 544707-04-2P 544707-06-4P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(polyethylene glycol aldehydes for conjugates with proteins)

RN 67665-19-4 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -(2-ethoxy-2-oxoethy1)- ω -methoxy-(9CI) (CA INDEX NAME)

MeO
$$CH_2-CH_2-O$$
 CH_2-C-OE

RN 92451-01-9 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-oxoethyl]- ω -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & \circ \\
 & \circ \\$$

RN 544706-94-7 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[2-[(3,3-diethoxypropyl)amino]-2-oxoethyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544706-96-9 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[3-[(4,4-dimethoxybutyl)amino]-3-oxopropyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544706-98-1 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(4,4-diethoxybutyl)amino]carbonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OEt} & \text{O} \\ \mid & \mid \\ \text{EtO-CH-(CH2)}_3 - \text{NH-C} & \text{O-CH2-CH2} \\ \end{array} \begin{array}{c} \text{OMe} \end{array}$$

RN 544707-00-8 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(4,4-dimethoxybutyl)amino]carbonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544707-01-9 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[2-[[[(3,3-diethoxypropyl)amino]carbonyl]amino]ethyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544707-04-2 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -[2-[[[3-(2,2-dimethy1-1,3-dioxolan-4-y1)propoxy]carbony1]amino]ethy1]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544707-06-4 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[3-(2,2-dimethyl-1,3-dioxolan-4-yl)propyl]- ω -methoxy- (9CI) (CA INDEX NAME)

IT 1659-31-0, Di-2-pyridyl carbonate 9004-74-4,

Methoxypolyethylene glycol

RL: RCT (Reactant); RACT (Reactant or reagent)

(polyethylene glycol aldehydes for conjugates with proteins)

RN 1659-31-0 CAPLUS

CN 2-Pyridinol, carbonate (2:1) (ester) (9CI) (CA INDEX NAME)

RN 9004-74-4 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -methyl- ω -hydroxy- (9CI) (CA INDEX NAME)

IT 135649-01-3P 146167-55-7P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(reaction with aminodiethoxypropane; polyethylene glycol aldehydes for conjugates with proteins)

RN 135649-01-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-ω-methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O \\
 & O \\$$

RN 146167-55-7 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[2-[[(2-pyridinyloxy)carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

IT 124661-64-9P 174569-25-6P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(reaction with aminodimethoxybutane; polyethylene glycol aldehydes for conjugates with proteins)

RN 124661-64-9 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -[(4-nitrophenoxy)carbony1]- ω -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & \hline \\ O - C & \hline \\ O - C + 2 - CH_2 - CH_2 \\ \hline \end{array} \begin{array}{c} O \\ n \end{array}$$

RN 174569-25-6 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]- ω -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & \circ \\
 & \circ \\$$

IT 58320-73-3P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(reaction with dioxolanedimethylpropanol; polyethylene glycol aldehydes for conjugates with proteins)

RN 58320-73-3 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -[(4-methylpheny1)sulfony1]- ω -methoxy- (9CI) (CA INDEX NAME)

$$\mathsf{MeO} = \begin{bmatrix} \mathsf{CH}_2 - \mathsf{CH}_2 - \mathsf{O} & \mathsf{S} \\ \mathsf{N} & \mathsf{N} \end{bmatrix}$$

IT 80506-64-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with dipyridiyl carbonate; polyethylene glycol aldehydes for conjugates with proteins)

RN 80506-64-5 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -(2-aminoethy1)- ω -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & \\ \text{MeO} & & \\ \hline \end{array} \begin{array}{c} \text{CH}_2 - \text{CH}_2 - \text{O} \\ \hline \end{array} \begin{array}{c} \text{CH}_2 - \text{CH}_2 - \text{NH}_2 \\ \end{array}$$

IT 67665-18-3P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(reaction with hydroxysuccinimide; polyethylene glycol aldehydes for conjugates with proteins)

RN 67665-18-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(carboxymethyl)- ω -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{MeO} & \hline & \text{CH}_2 - \text{CH}_2 - \text{O} \\ \hline & \text{n} \end{array}$$

IT . 125220-94-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with hydroxysuccinimide; polyethylene glycol aldehydes for conjugates with proteins)

RN 125220-94-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(2-carboxyethyl)- ω -methoxy- (9CI) (CA INDEX NAME)

IT 6066-82-6, N-Hydroxysuccinimide
RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction with methoxypolyethylene glycol acetic acid; polyethylene glycol aldehydes for conjugates with proteins)

RN 6066-82-6 CAPLUS

CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)

IT 544707-03-1P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(reaction with methoxypolyethylene glycol aminoethyl ether; polyethylene glycol aldehydes for conjugates with proteins)

RN 544707-03-1 CAPLUS

CN 1,3-Dioxolane-4-propanol, 2,2-dimethyl-, 4-nitrobenzoate (9CI) (CA INDEX NAME)

IT 19060-15-2

RL: RCT (Reactant); RACT (Reactant or reagent) (reaction with methoxypolyethylene glycol succinimidyl acetal; polyethylene glycol aldehydes for conjugates with proteins)

RN 19060-15-2 CAPLUS

CN 1-Butanamine, 4,4-dimethoxy- (9CI) (CA INDEX NAME)

IT 41365-75-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with methoxypolyethylene glycol succinimidyl acetate;
polyethylene glycol aldehydes for conjugates with proteins)

RN 41365-75-7 CAPLUS

CN 1-Propanamine, 3,3-diethoxy- (9CI) (CA INDEX NAME)

IT 105-36-2, Ethyl bromoacetate 7693-46-1, 4-Nitrophenylchloroformate 32315-10-9, Triphosgene

RL: RCT (Reactant); RACT (Reactant or reagent) (reaction with methoxypolyethylene glycol; polyethylene glycol aldehydes for conjugates with proteins)

105-36-2 CAPLUS RN

Acetic acid, bromo-, ethyl ester (6CI, 8CI, 9CI) (CA INDEX NAME) CN

7693-46-1 CAPLUS RN

Carbonochloridic acid, 4-nitrophenyl ester (9CI) (CA INDEX NAME) CN

RN32315-10-9 CAPLUS

Methanol, trichloro-, carbonate (2:1) (9CI) (CA INDEX NAME) CN

6318-30-5

RE: RCT (Reactant); RACT (Reactant or reagent) (reaction with nitrophenylchloroformate; polyethylene glycol aldehydes for conjugates with proteins)

RN 6318-30-5 CAPLUS

CN1,3-Dioxolane-4-propanol, 2,2-dimethyl- (9CI) (CA INDEX NAME)

$$Me$$
O
(CH₂)₃-OH

ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:142840 CAPLUS

DOCUMENT NUMBER:

140:181998

ENTRY DATE:

Entered STN: 22 Feb 2004

TITLE:

Novel monofunctional polyethylene glycol aldehydes

INVENTOR(S):

Rosen, Perry; Nho, Kwang

PATENT ASSIGNEE (S): Sun Bio, Inc., USA

SOURCE:

U.S. Pat. Appl. Publ., 16 pp., Cont.-in-part of U.S.

Ser. No. 303,260. CODEN: USXXCO

DOCUMENT TYPE:

Patent English

LANGUAGE:

INT. PATENT CLASSIF.:

MAIN:

C08G065-00

US PATENT CLASSIF .:

528230000; 528250000 35-8 (Chemistry of Synthetic High Polymers)

CLASSIFICATION:

Section cross-reference(s): 63

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
					22222
US 2004034188	A1	20040219	US 2003-431294		20030507
US 6916962	В2	20050712	•		
KR 2003048293	Α	20030619	KR 2001-78244		20011211
US 2003153694	A1	20030814	US 2002-303260		20021125
US 2004122164	A1	20040624	US 2003-661268		20030912
US 2004147687	A1	20040729	US 2003-715607		20031118 <
PRIORITY APPLN. INFO.:			KR 2001-78244	Α	20011211.
			US 2002-348452P	P	20020116
			US 2002-381503P	P	20020517
			US 2002-407741P	P	20020903
			US 2002-303260	A2	20021125
			US 2003-431294	A2	20030507
			US 2003-661268	A2	20030912

$D\Delta TFMT$	CLASSIFICATION	CODES.
PAIGNI	CHAPSILICATION	CODES

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004034188	ICM	C08G065-00
	INCL	528230000; 528250000
US 2004034188	NCL	528/230.000; 528/250.000
	ECLA	C08G065/324; C08G065/329; C08G065/331; C08G065/333U
US 2003153694	NCL	525/523.000; 558/260.000; 560/157.000; 564/060.000
	ECLA	C08G065/329; C08G065/331; C08G065/333U
US 2004122164	NCL	525/054.100; 528/230.000; 525/526.000
	ECLA	C08G065/324; C08G065/329; C08G065/331; C08G065/333U
US 2004147687	NCL	525/389.000; 525/403.000
	ECLA	C08G065/324; C08G065/329; C08G065/331; C08G065/333U <

ABSTRACT:

The present invention provides novel monofunctional polyethylene glycol aldehydes for the pegylation of therapeutically active proteins. The pegylated protein conjugates that are produced, retain a substantial portion of their therapeutic activity and are less immunogenic than the protein from which the conjugate is derived. New syntheses for preparing such aldehydes are described.

SUPPL. TERM:

polyethylene glycol aldehyde therapeutic active protein

pegylation

INDEX TERM:

Polyoxyalkylenes, preparation

ROLE: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (aldehyde derivs.; novel monofunctional polyethylene glycol aldehydes for pegylation of therapeutically active

proteins)

INDEX TERM:

Proteins

ROLE: THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

(pegylation of; novel monofunctional polyethylene glycol aldehydes for pegylation of therapeutically active

```
proteins)
INDEX TERM:
                 544706-95-8P
                   ROLE: IMF (Industrial manufacture); PREP (Preparation)
                      (novel monofunctional polyethylene glycol aldehydes for
                      pegylation of therapeutically active proteins)
INDEX TERM:
                 6318-30-5P 58320-73-3P 67665-18-3P
                   , Methoxypolyethylene glycol acetic acid 67665-19-4P
                   , Methoxypolyethylene glycol ethyl acetate
                   124661-64-9P 135649-01-3P
                   146167-55-7P 544706-94-7P
                   544706-96-9P 544707-00-8P
                   544707-01-9P 544707-03-1P
                   544707-04-2P 544707-06-4P
                   658083-74-0P 658083-75-1P
                   ROLE: IMF (Industrial manufacture); RCT (Reactant); PREP
                   (Preparation); RACT (Reactant or reagent)
                      (novel monofunctional polyethylene glycol aldehydes for
                      pegylation of therapeutically active proteins)
INDEX TERM:
                 314065-74-2DP, Acrylic acid-ethylene oxide graft
                   copolymer methyl ether, ester with N-hydroxysuccinimide,
                   displacement reaction products with 1-amino-4,4-
                   dimethoxybutane, deacetalized compds. 533881-58-2P
                   544706-97-0P 544706-99-2P
                   544707-02-0P 544707-05-3P
                   544708-06-7P
                   ROLE: IMF (Industrial manufacture); THU (Therapeutic use);
                   BIOL (Biological study); PREP (Preparation); USES (Uses)
                      (novel monofunctional polyethylene glycol aldehydes for
                      pegylation of therapeutically active proteins)
INDEX TERM:
                 67-64-1, Acetone, reactions 98-59-9, Tosyl
                   chloride 105-36-2, Ethyl bromoacetate
                   1659-31-0, Di-2-pyridyl carbonate 6066-82-6
                   , N-Hydroxysuccinimide 7693-46-1, 4-Nitrophenyl
                   chloroformate 9004-74-4, Methoxypolyethylene
                  glycol 14697-46-2, Pentane-1,2,5-triol
                   19060-15-2 32315-10-9, Triphosgene
                   41365-75-7 80506-64-5 125220-94-2
                   , Methoxypolyethylene glycol propionic acid
                   152552-24-4, Acrylic acid-methoxypolyethylene glycol
                   graft copolymer 314065-74-2, Acrylic acid-ethylene
                   oxide graft copolymer methyl ether 314065-74-2D,
                   Acrylic acid-ethylene oxide graft copolymer methyl ether,
                   ester with N-hydroxysuccinimide
                   ROLE: RCT (Reactant); RACT (Reactant or reagent)
                      (novel monofunctional polyethylene glycol aldehydes for
                      pegylation of therapeutically active proteins)
ΙT
     544706-95-8P
     RL: IMF (Industrial manufacture); PREP (Preparation)
        (novel monofunctional polyethylene glycol aldehydes for pegylation of
        therapeutically active proteins)
   544706-95-8 CAPLUS
RN
     Poly(oxy-1,2-ethanediyl), \alpha-methyl-\omega-[2-oxo-2-[(3-
CN
     oxopropyl)amino]ethoxy]- (9CI) (CA INDEX NAME)
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um a managamang mental dan dan silahatan silah salah silah salah s

$$OHC-CH_2-CH_2-NH-C-CH_2-O-CH_2-CH_2-CH_2-O-NH-N$$

IT 6318-30-5P 58320-73-3P 67665-18-3P,

Methoxypolyethylene glycol acetic acid 67665-19-4P,

Methoxypolyethylene glycol ethyl acetate 124661-64-9P

135649-01-3P 146167-55-7P 544706-94-7P

544706-96-9P 544707-00-8P 544707-01-9P

544707-03-1P 544707-04-2P 544707-06-4P

658083-74-0P 658083-75-1P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(novel monofunctional polyethylene glycol aldehydes for pegylation of

therapeutically active proteins)

RN 6318-30-5 CAPLUS

CN

1,3-Dioxolane-4-propanol, 2,2-dimethyl- (9CI) (CA INDEX NAME)

Me
$$O$$
 (CH₂)₃-OH

RN 58320-73-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[(4-methylphenyl)sulfonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

$$\mathsf{Meo} = \begin{bmatrix} \mathsf{CH}_2 - \mathsf{CH}_2 - \mathsf{O} & \mathsf{I} & \mathsf{I} \\ \mathsf{In} & \mathsf{II} & \mathsf{II} \\ \mathsf{O} & \mathsf{III} & \mathsf{III} \\ \mathsf{O} & \mathsf{O} & \mathsf{III} \\ \mathsf{O} & \mathsf{O} & \mathsf{III} \\ \mathsf{O} & \mathsf{O} & \mathsf{O} \\ \mathsf{O} \\ \mathsf{O} & \mathsf{O} \\ \mathsf{O} & \mathsf{O} \\ \mathsf{O} \\ \mathsf{O} & \mathsf{O} \\ \mathsf{O} \\$$

RN 67665-18-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(carboxymethyl)- ω -methoxy- (9CI) (CA INDEX NAME)

$$\texttt{MeO} = \begin{bmatrix} \texttt{CH}_2 - \texttt{CH}_2 - \texttt{O} & \texttt{In} \\ \texttt{n} & \texttt{CH}_2 - \texttt{CO}_2 \texttt{H} \end{bmatrix}$$

RN 67665-19-4 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(2-ethoxy-2-oxoethyl)- ω -methoxy-(9CI) (CA INDEX NAME)

MeO
$$CH_2$$
 CH_2 OH_2 $OH_$

RN 124661-64-9 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -[(4-nitrophenoxy)carbony1]- ω -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O \\
 & C \\
 & O \\
 & C \\
 & O \\
 & C \\
 & O \\$$

RN 135649-01-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & \circ \\
 & \circ \\$$

RN 146167-55-7 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[2-[[(2-pyridinyloxy)earbonyl]amino]ethoxy]- (9CI) (CA-INDEX-NAME)

RN 544706-94-7 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[2-[(3,3-diethoxypropyl)amino]-2-oxoethyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544706-96-9 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -[3-[(4,4-dimethoxybuty1)amino]-3-

oxopropyl]-ω-methoxy- (9CI) (CA INDEX NAME)

MeO
$$\sim$$
 CH₂ \sim CH₂ \sim CH₂ \sim CH₂ \sim CH \sim OMe \sim CH₂ \sim CH \sim CH₂ \sim CH \sim OMe \sim CH₂ \sim CH \sim CH₂ \sim C

RN 544707-00-8 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(4,4-dimethoxybutyl)amino]carbonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544707-01-9 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -[2-[[[(3,3-diethoxypropy1)amino]carbony1]amino]ethy1]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 544707-03-1 CAPLUS

CN 1,3-Dioxolane-4-propanol, 2,2-dimethyl-, 4-nitrobenzoate (9CI) (CA INDEX NAME)

RN 544707-04-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), $\alpha-[2-[[[3-(2,2-dimethyl-1,3-dioxolan-4-yl)propoxy]carbonyl]amino]ethyl]-<math>\omega$ -methoxy- (9CI) (CA INDEX NAME)

RN 544707-06-4 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[3-(2,2-dimethyl-1,3-dioxolan-4-yl)propyl]- ω -methoxy- (9CI) (CA INDEX NAME)

Me O (CH₂)₃
$$-$$
 O CH₂ - CH₂ $-$ OMe

RN 658083-74-0 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[3-(2,5-dioxo-1-pyrrolidinyl)-2-oxopropyl]- ω -methoxy- (9CI) (CA INDEX NAME)

RN 658083-75-1 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(3,3-diethoxypropyl)amino]carbonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OEt} & \text{O} \\ \mid & \mid & \\ \text{EtO-CH-CH}_2\text{-CH}_2\text{-NH-C} & \text{O-CH}_2\text{-CH}_2 & \text{OMe} \end{array}$$

IT 314065-74-2DP, Acrylic acid-ethylene oxide graft copolymer methyl ether, ester with N-hydroxysuccinimide, displacement reaction products with 1-amino-4,4-dimethoxybutane, deacetalized compds.

533881-58-2P 544706-97-0P 544706-99-2P 544707-02-0P 544707-05-3P 544708-06-7P

RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(novel monofunctional polyethylene glycol aldehydes for pegylation of therapeutically active proteins)

RN 314065-74-2 CAPLUS

CN 2-Propenoic acid, polymer with oxirane, methyl ether, graft (9CI) (CA INDEX NAME)

CM 1

CRN 67-56-1 CMF C H4 O

H3C-OH

CM 2

CM 3

CRN 79-10-7 CMF C3 H4 O2

CM 4

CRN 75-21-8 CMF C2 H4 O



RN 533881=58=2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -(4-oxobutoxy)- (9CI) (CA INDEX NAME)

OHC-
$$(CH_2)_3$$
-O-CH₂-CH₂-O-Ne

RN 544706-97-0 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -methy1- ω -[3-oxo-3-[(4-oxobuty1)amino]propoxy]- (9CI) (CA INDEX NAME)

RN 544706-99-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(4-oxobutyl)amino]carbonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

OHC-
$$(CH_2)_3$$
-NH- C - CH_2 - CH_2 - CH_2 - CH_2 - D - D

RN 544707-02-0 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α -methyl- ω -[2-[[[(3-oxopropyl)amino]carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

RN 544707-05-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -methyl- ω -[2-[[(4-oxobutoxy)carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

OHC-
$$(CH_2)_3$$
-O-C-NH- CH_2 - CH_2 -O-CH₂- CH_2 -O-Me

RN 544708-06-7 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[[(3-oxopropyl)amino]carbonyl]- ω -methoxy- (9CI) (CA INDEX NAME)

OHC-
$$CH_2$$
- CH_2 - NH - C - CH_2 - CH_2 - CH_2 - DM

RN 67-64-1 CAPLUS

CN 2-Propanone (9CI) (CA INDEX NAME)

CN Benzenesulfonyl chloride, 4-methyl- (9CI) (CA INDEX NAME)

RN 105-36-2 CAPLUS

CN Acetic acid, bromo-, ethyl ester (6CI, 8CI, 9CI) (CA INDEX NAME)

RN 1659-31-0 CAPLUS

CN 2-Pyridinol, carbonate (2:1) (ester) (9CI) (CA INDEX NAME)

RN 6066-82-6 CAPLUS

CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)

RN 7693-46-1 CAPLUS

CN Carbonochloridic acid, 4-nitrophenyl ester (9CI) (CA INDEX NAME)

RN 9004-74-4 CAPLUS

CN Poly(oxy-1,2-ethanediy1), α-methyl-ω-hydroxy- (9CI) (CA INDEX NAME)

HO
$$CH_2$$
 CH_2 OH_2 OH_3

RN 14697-46-2 CAPLUS

CN 1,2,5-Pentanetriol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

RN 19060-15-2 CAPLUS

CN 1-Butanamine, 4,4-dimethoxy- (9CI) (CA INDEX NAME)

RN 32315-10-9 CAPLUS

CN Methanol, trichloro-, carbonate (2:1) (9CI) (CA INDEX NAME)

RN 41365-75-7 CAPLUS

CN 1-Propanamine, 3,3-diethoxy- (9CI) (CA INDEX NAME)

RN 80506-64-5 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(2-aminoethyl)- ω -methoxy- (9CI) (CA INDEX NAME)

MeO
$$CH_2-CH_2-O$$
 $CH_2-CH_2-NH_2$

RN 125220-94-2 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(2-carboxyethyl)- ω -methoxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & \\ & & \\ & & \\ \end{array} \text{MeO} \begin{array}{c} & \\ & \\ \end{array} \text{CH}_2 - \text{CH}_2 - \text{CO}_2 \text{H} \\ \end{array}$$

RN 152552-24-4 CAPLUS

CN 2-Propenoic acid, polymer with α-methyl-ω-hydroxypoly(oxy-1,2-ethanediyl), graft (9CI) (CA INDEX NAME)

CM 1

CRN 9004-74-4

CMF (C2 H4 O)n C H4 O

CCI PMS

CM 2

CRN 79-10-7 CMF C3 H4 O2

RN 314065-74-2 CAPLUS

CN 2-Propenoic acid, polymer with oxirane, methyl ether, graft (9CI) (CA INDEX NAME)

CM 1

CRN 67-56-1

CMF C H4 O

 $_{
m H_3C-OH}$

CRN 112344-11-3

CMF (C3 H4 O2 . C2 H4 O)x

CCI PMS

CM 3

CRN 79-10-7 CMF C3 H4 O2

and and the contract of the co

CM 4

CRN 75-21-8 CMF C2 H4 O



RN314065-74-2-CAPLUS

CN 2-Propenoic acid, polymer with oxirane, methyl ether, graft (9CI) (CA INDEX NAME)

CM 1

CRN 67-56-1 CMF C H4 O

нзс-он

CM 2

CRN 112344-11-3

CMF (C3 H4 O2 . C2 H4 O) x

CCI PMS

011-----

CRN 79-10-7 CMF C3 H4 O2

CM 4

CRN 75-21-8 CMF C2 H4 O

